PRINTER RUSH
(PTO ASSISTANCE)

Application : 10/019,199 **Examiner :** G.S.Kishore **GAU :** 1615

From: S.Winslow **Location:** (IDC) FMF FDC **Date:** 1-18-06

Tracking #: EPM 10/019,199 Week Date: 10-24-05

DOC CODE	DOC DATE	MISCELLANEOUS
☐ 1449		☐ Continuing Data
☐ IDS		☐ Foreign Priority
☐ CLM		☐ Document Legibility
☐ IIFW		☐ Fees
☐ SRFW		☐ Other
☐ DRW		
☐ OATH		
☐ 312		
☒ SPEC	12-20-01	

[RUSH] **MESSAGE:** Spec p. 15, line 18, missing Ser. No.

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REV 10/04

selection of these characteristics can be used to control the characteristics of the product multilamellar vesicles. These characteristics include:

(1) the inclusion of a charged lipid in the preformed lipid vesicles with a charge opposite that of the therapeutic agent;

(2) the inclusion of a modified lipid in an amount sufficient to retard aggregation, but not enough to prevent aggregation. In the case of PEG-CerC_{14}, this amount was found to be on the order of 2.5 to 10%;

(3) the inclusion in the destabilizing solvent of a destabilizing agent (such as ethanol or detergent) in an amount that destabilizes but does not disrupt the preformed lipid vesicles; and

(4) performing the assembly of the fully lipid-encapsulated therapeutic agent particles at a temperature where the aggregation and the entrapment step are not decoupled. In general this will require operation in a temperature range of room temperature (~20°C) or above, depending on the concentration of destabilizing agent and the lipid composition.

The method of the invention can be practiced using conventional mixing apparatus. For large scale manufacture, however, it may be desirable to use a specifically adapted apparatus which is described in a concurrently filed PCT application, entitled "Methods and Apparatus for Preparation of Lipid Vesicles", ~~Serial No. Not yet assigned~~ PCT/CA00/00842, filed 14 July 2000, ~~(Attorney Docket No. 80472-6)~~ which is incorporated herein by reference.

The method of the invention will now be further described with reference to the following, non-limiting examples.

Examples

Materials used in the following examples are supplied as follows:

The phosphorothioate antisense oligodeoxynucleotides and plasmid DNA used in this study were provided by Inex Pharmaceuticals (Burnaby, BC, Canada). The mRNA targets and sequences of the oligonucleotides are as follows:

human c-myc, 5'-TAACGTTGAGGGGCAT-3' (Seq ID No. 1);

human ICAM-1, 5'-GCCCAAGCTGGCATCCGTCA-3' (SEQ ID No. 2); and

FITC-labeled human EGFR, 5'-CCGTGGTCATGCTCC-3' (SEQ ID No. 3).

1,2-Distearoyl-sn-glycero-3-phosphocholine (DSPC) was purchased from Northern Lipids (Vancouver, BC, Canada) and 1,2-dioleoyl-3-dimethylammoniumpropane